PRELIMINARY AND SHORT REPORTS

ISONIAZID* IN THE TREATMENT OF CHRONIC DISCOID LUPUS ERYTHEMATOSUS

Report of Three Cases†

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With modern therapeutic measures, chronic discoid lupus erythematosus gives a good prognosis regarding eventual clearing of lesions although some cases resist the usual methods of treatment. Therefore, and because of the tendency to recur, the search for better therapeutic modalities continues.

When isoniazid was reported effective against pulmonary tuberculosis (1, 2, 3), we decided to try it in tuberculoderms and in sarcoidosis. Obermayer et al. (4) reported a case of lupus vulgaris of forty years duration which was cured by isoniazid orally in a dosage of 4 mg/kg.

We further had the opportunity to observe 3 cases of chronic discoid lupus erythematosus which we treated with this remedy. The course of these 3 patients constitutes the following report.

Case 1. A 46-year-old Chinese man had noted a small, progressively enlarging, dark-red area on his left cheek for about three years before he came under our observation in March 1952. The lesion consisted of a pink-red, sharply outlined, horse-shoe shaped, infiltrated plaque about 4.5 cm in diameter. There was adherent grayish scaliness, involving the left cheek and pre-auricular lesions. Some telangiectasia was present. There was no atrophy, deep plugging, or clear evidence of scarring. The patient complained of moderate pruritus. Previous therapy, including bismuth, had been without benefit.

On March 14, 1952, histopathologic confirmation of the clinical diagnosis of chronic discoid lupus erythematosus was obtained. The biopsy revealed hyperkeratosis with follicular plugging and slight thickening of the granular and prickle-cell layers. The basal cell layer showed degeneration and disorganization. There was a small, lymphocytic infiltration about the glands and some of these infiltrating cells were also present in the lowermost layers of the epidermis. The cutis showed vascular dilatation with a similar perivascular infiltrate. There were edema of the collagen bundles and basophilic changes in the collagen and elastic tissue.

Isoniazid therapy was instituted orally on March 20. The initial daily dose of 1 mg/kg was increased to 2 mg/kg after one week. After three more weeks the daily dose was raised to 3 mg/kg and finally to 4 mg/kg, three months after initiation of the medication. A week later the patient complained of gastric distress relieved by decreasing, and recurring with resumption of the higher dose. Therefore, a daily dose level of 3 mg/kg was maintained until December 1 (total isoniazid therapy—36 weeks; total intake—40.95 gm).

A hemogram done prior to initiating isoniazid revealed a moderate, hypochromic, microcytic anemia (RBC 3,040,000; hemoglobin (Sahli) 65%). Gradual improvement, as shown by repeated blood counts, brought the erythrocyte count to 4,460,000 and the hemoglobin to 81% after six months of treatment with isoniazid. The leukocyte counts, urinalyses and sedimentation rates were within normal range initially and throughout therapy.

Within one week of initiation of isoniazid, there was slight, but definite improvement

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consisting of a decrease in the redness and swelling of the lesion. Further gradual improvement led to "whitening" of the lower pole of the lesion, suggestive of the beginning of scarring, typical of lupus erythematosus.

On October 31 a biopsy performed at the only residual, faintly pink corner of the lesion showed thinning of the entire epidermis with no definite basal cell layer, atrophy of the glandular structures, very few lymphoid cells, and replacement of the usually distinguishable features of the cutis by relatively amorphous connective tissue. Although no clinical or laboratory activity was believed present, isoniazid was continued for one month.

Case 2. A 20-year-old colored female had noticed for several years small reddish lesions on the forehead, eyelids, left cheek, and right forearm. These enlarged and increased in number very slowly to 6 lesions. When first seen at our clinic, all lesions were small, infiltrated, reddish-brown plaques with some atrophy and plugging. Histopathologic confirmation of the clinical diagnosis of chronic discoid lupus erythematosus could not be obtained because the patient refused to permit a biopsy. For a period of two months treatment with liver and subsequently with bismuth injections produced no improvement. On March 22, 1952, the patient permitted a biopsy which confirmed the diagnosis, showing moderate hyperkeratosis with follicular and epidermal plugging, thinning of all the other layers of the epidermis and a liquefaction-degeneration and disorganization of the basal cell layer, a patchy perivascular and perifollicular lymphocytic infiltration, slight basophilic change of collagen and elastic tissue and slight edema of the uppermost portion of the cutis with some small vessel dilatation. Oral isoniazid therapy was instituted on March 21 and continued until December 1. The initial daily dose of 1 mg/kg was increased gradually as in Case 1. Again, 3 mg/kg was the daily dose tolerated with only an occasional complaint of slight epigastric discomfort or transient headache. The total isoniazid dose was 37.45 gm. Prior to beginning the isoniazid therapy, there was a mild hypochromic, microcytic anemia which improved slightly during therapy. Leukocyte counts, including differential counts, sedimentation rates and urinalyses were normal initially and throughout treatment. Under therapy with isoniazid all lesions improved markedly, but only two cleared completely. On October 24 a biopsy taken from the same lesion from which the original specimen had been taken (and which showed only a moderate degree of improvement), revealed slight hyperkeratosis with superficial plugging of the epidermis; the few visible glandular structures were atrophic and not plugged. All the layers were thinned, with the basal cell layer "irregular and indefinite." The corium was atrophic with a few small foci of lymphocytic cells about the vessels and vestige of one follicle. Basophilic changes of the cutis were slight, but cellular structure was indistinct.

Isoniazid was discontinued on December 1 to see whether the improvement would persist without therapy.

Case 3. A 31-year-old colored female had had typical lesions of chronic discoid lupus erythematosus for more than one year on the cheeks, forehead, and left post-auricular area. A biopsy on March 7, 1952, revealed findings similar to those of the first two cases. Isoniazid was instituted on March 21 and continued until October 3. In general, the daily dose was 3 mg/kg, although for six weeks she received 4 mg/kg daily (total isoniazid intake —29.15 gm). At the higher dose level, the patient experienced transient headache, slight gaseous distress and fatigue. This patient too had a moderate hypochromic, microcytic anemia which improved considerably during therapy.

There was considerable clinical improvement of all lesions beginning promptly after the institution of isoniazid and continuing throughout therapy. Unfortunately, the patient became irregular in her clinic attendance and could not be followed after October 3, so that no post-medication biopsy was obtained.

SUMMARY AND COMMENTS

Three cases of proven chronic discoid lupus erythematosus, all with progressing lesions of long duration, were treated with isoniazid with a high degree of success. Clinical improvement began shortly after the initiation of medication and progressed to complete inactiva-

tion in one patient, while the other two patients showed complete inactivation of some lesions and marked improvement in the others.

Isoniazid was used empirically. Histopathologic studies showed without doubt that involutional changes occurred during the administration of isoniazid. The microcytic, hypochromic anemias seen in all three patients improved during isoniazid therapy.

The optimal daily dose in these ambulatory patients was 3 mg/kg. At this dosage the only reactions observed were mild transient gastric complaints and mild headaches.

While we used Atabrine® experimentally and are impressed with the excellent results we obtained as well as with those recently described by others (5, 6, 7), we feel that isoniazid with its striking clinical and pathological evidences of effectiveness should be considered as an alternative therapeutic modality in the treatment of discoid lupus erythematosus.

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